Our Ancestors' Ghosts:
Ancestral Exposure to Stress Epigenetically Programs Preterm Birth Risk and Health Outcomes

Gerlinde A. S. Metz

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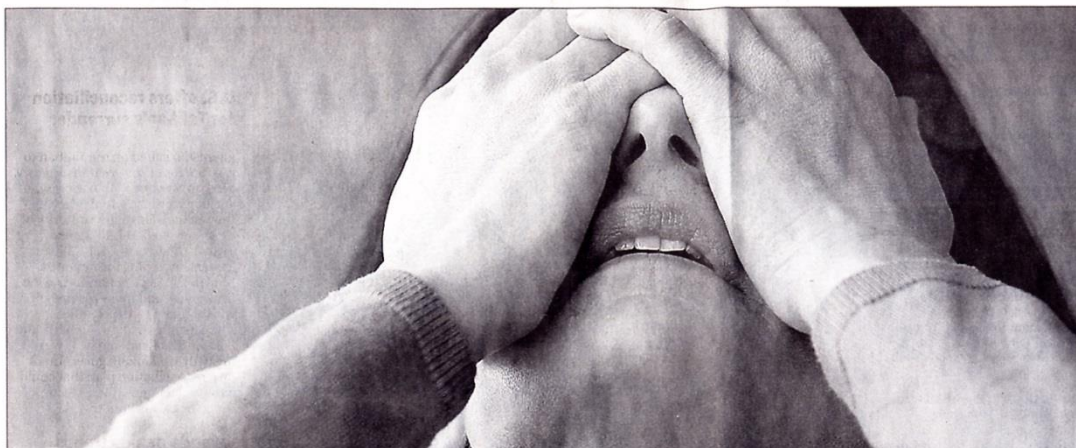
Alberta, Canada



Blood cells from women who spent years caring for a disabled child 'were genetically about a decade older than those from peers who had much less caretaking exper

Severe distress accelerates aging

The findings by U.S. researchers are the first to link psychological stress directly to biological age

BY BENEDICT CAREY

Some stressful events seem to turn a person's hair grey overnight.

Now a team of researchers has found that severe emotional distress — like that caused by divorce, the loss of a job, or caring for an ill child or parent — may speed

being stressed can add years to a person's biological age.

Though doctors have linked chronic psychological stress to weakened immune function and an increased risk of catching colds, among other things, they are still trying to understand how tension damages or weakens tissue. The new research suggests a new way

dency to put on fat, to develop heart disease and diabetes."

In the experiment, Dr. Elissa Epel and Dr. Elizabeth Blackburn of the University of California at San Francisco led a team of researchers who analyzed blood samples from 58 young and middle-aged mothers, 39 of them caring for a child with a chronic disorder such as autism or cerebral palsy. Using genetic techniques, the doctors examined the DNA of white blood cells, which are central to the body's immune response to infection.

The scientists focused on a piece of DNA, called the telomere, at the

the telomere gets so short that the cell is effectively retired and no longer able to replicate.

People born with a genetic disease called dyskeratosis congenita, which causes accelerated shortening of telomeres, die young, usually by middle age, most often as a result of complications from weakened immunity.

Change in telomere length over time, in short, is thought to be a rough measure of a cell's age, its vitality.

And when the researchers compared the DNA of mothers caring for disabled children, they found a

Dr. Blackburn, a
chemistry and bi

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Category: LifeH
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Stress and depression are major causes of premature births | Mail Online Page 1 of 2

Mail Online

Stress and depression are major causes of premature births

Stress and depression in pregnancy is a major cause of premature birth, experts have warned.

Research shows that stress hormones - which play a crucial role in the development of the unborn baby - shoot up in women who are depressed during pregnancy.

High levels of these hormones are involved in triggering labour, leading scientists to believe they could be behind many of the 45,000 premature births that occur in the UK each year - with potentially devastating results.

Premature babies - born before 37 weeks of pregnancy - are more likely to die in the first weeks of life and are at risk of a host of health problems, with one in ten developing a permanent disability such as lung disease, cerebral palsy, blindness or deafness.

While many of these early births can be explained by medical reasons, such as infection or complications with the pregnancy,

Mother's stress, depression affects unborn child, researchers say

Studies indicate the infants are at greater risk for learning, behavioural problems

BY LAURIE TARKAN

By listening intently to movements and heartbeats, researchers are finding that the fetuses of mothers who are stressed or depressed respond differently from those of emotionally healthy women.

After birth, studies indicate, these infants have a significantly increased risk of developing learning and behavioural problems, and may themselves be more vulnerable to depression or anxiety as they age.

The studies, researchers caution, are preliminary. Stress or depression during a mother's pregnancy is only one among many influences that affect an infant's development. Even among mothers who are depressed or highly stressed, the rate of emotional and behavioural problems in children is still very low.

"The last thing pregnant women need is to have something else to worry about," said Dr. Janet DiPietro, a developmental psychologist at the Johns Hopkins University Bloomberg School of Public Health.

The studies reflect growing evidence that stress and depression can have early and lasting effects on a child's life. If the findings hold up, experts say, they could eventually lead obstetricians, midwives and other health professionals who care for pregnant women to include mental health screening as a routine part of prenatal examinations.

in brain chemistry and behaviour. For example, rat pups exposed prenatally to elevated levels of the stress hormone corticosterone were born with reduced numbers of corticosterone receptors in the brain, and showed exaggerated responses to stress.

In humans, there is convincing evidence that mothers who are stressed in pregnancy are more likely to give birth preterm or to infants with low birth weights.

In recent years, scientists have begun studying how fetuses respond to their mothers' anxiety or depression, the emotional health of the infants after birth and how they fare later in childhood. Some studies have offered unusual glimpses into the symbiotic relationship between a mother and a developing child.

Dr. Monk has looked at the increase and decrease in fetal heart rate when the mother is under stress.

In one study, women in the third trimester of pregnancy went through psychological screening for depression and anxiety. They were then asked to perform a series of stress-inducing computer tasks. As expected, all the women showed increased heart rate, respiration and blood pressure. Fetal responses were more varied. The fetuses of mothers who were depressed or had anxious personality styles showed increased heart rates. In contrast, the heart rates of fetuses

'Prenatal care is an optimal tim

ing, or to a jolt of stress hormone

Dr. Monk said depressed wom
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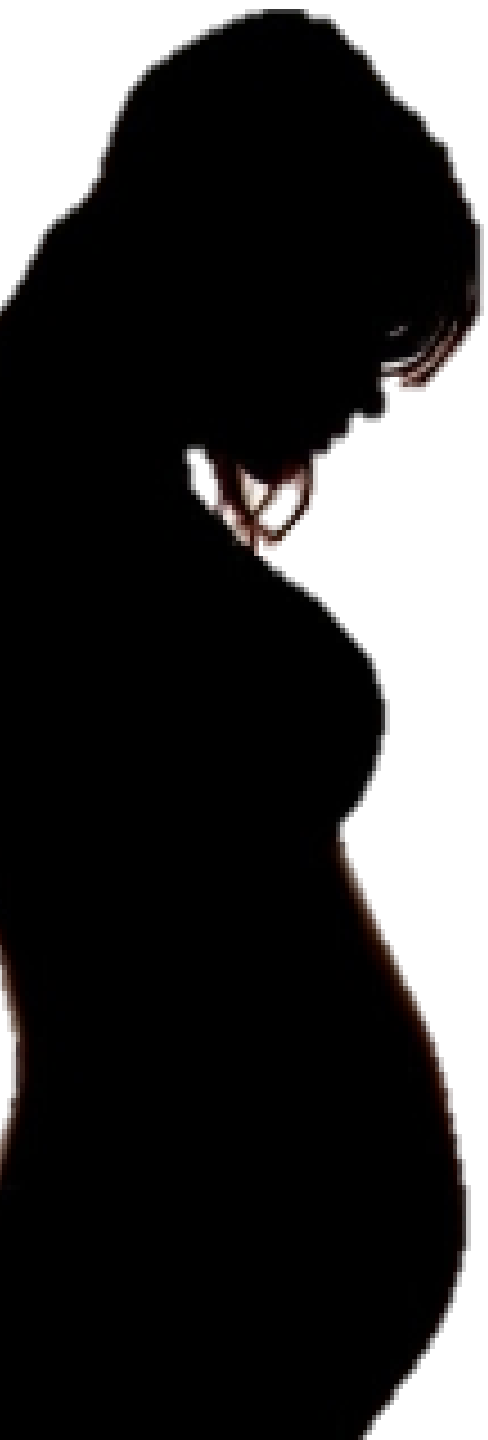
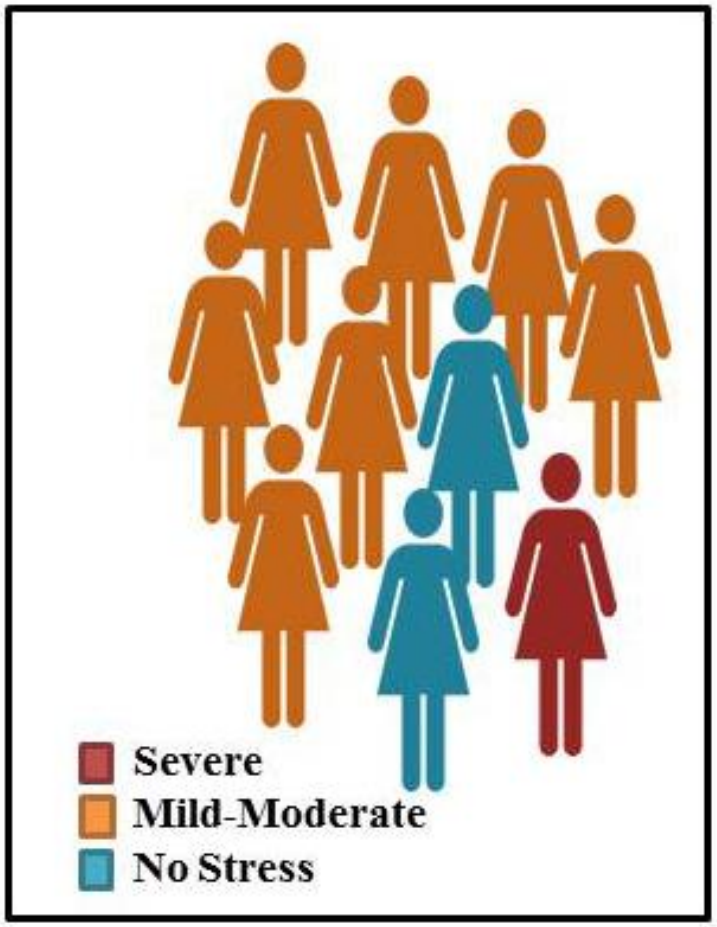
levels of stress hormones such
cortisol. She speculated that th



Programming of the Stress Response



Stress generates a footprint that travels
from one generation to the next…

Stress generates a footprint that travels from one generation to the next…

HYPOTHESIS: Ancestral Stress Programs Maternal and Offspring Health Trajectories

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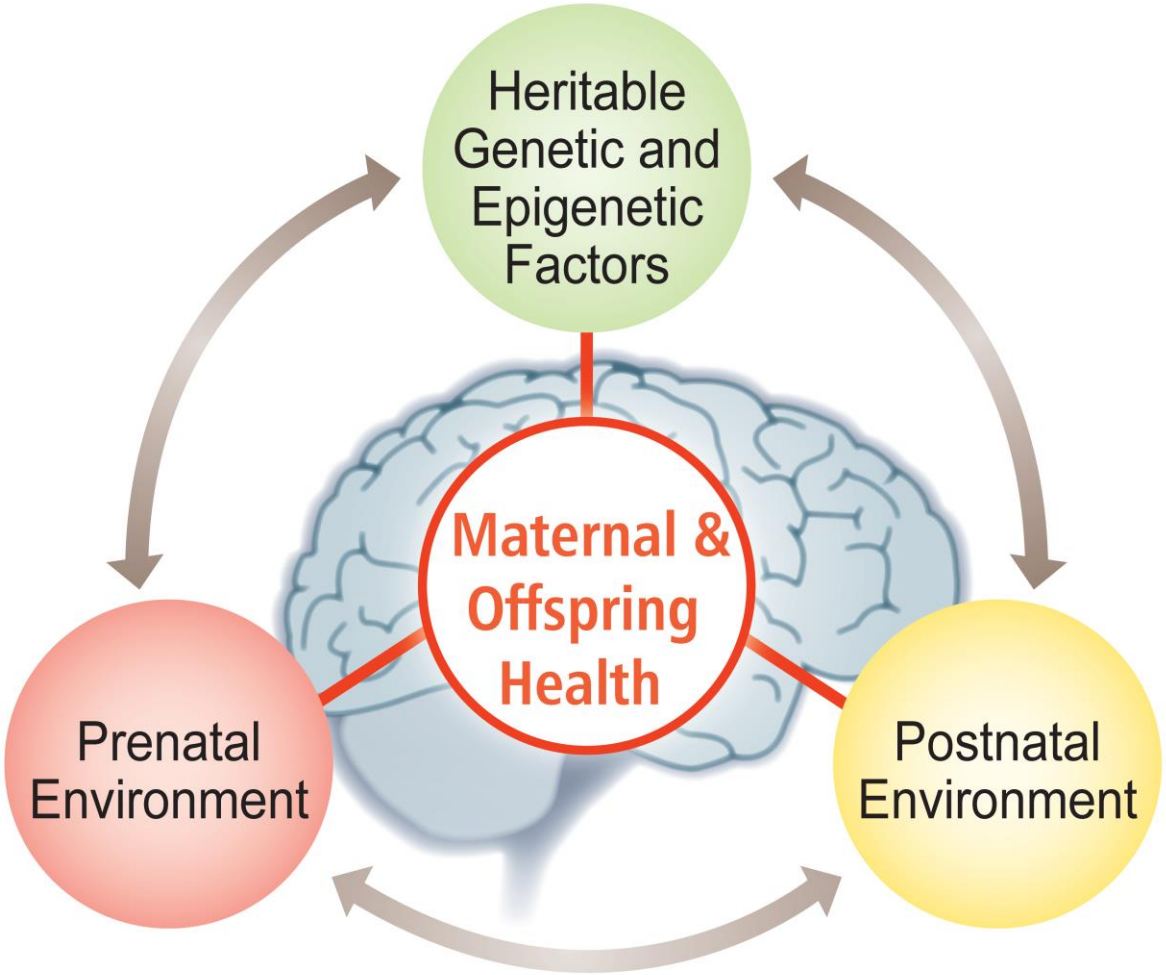

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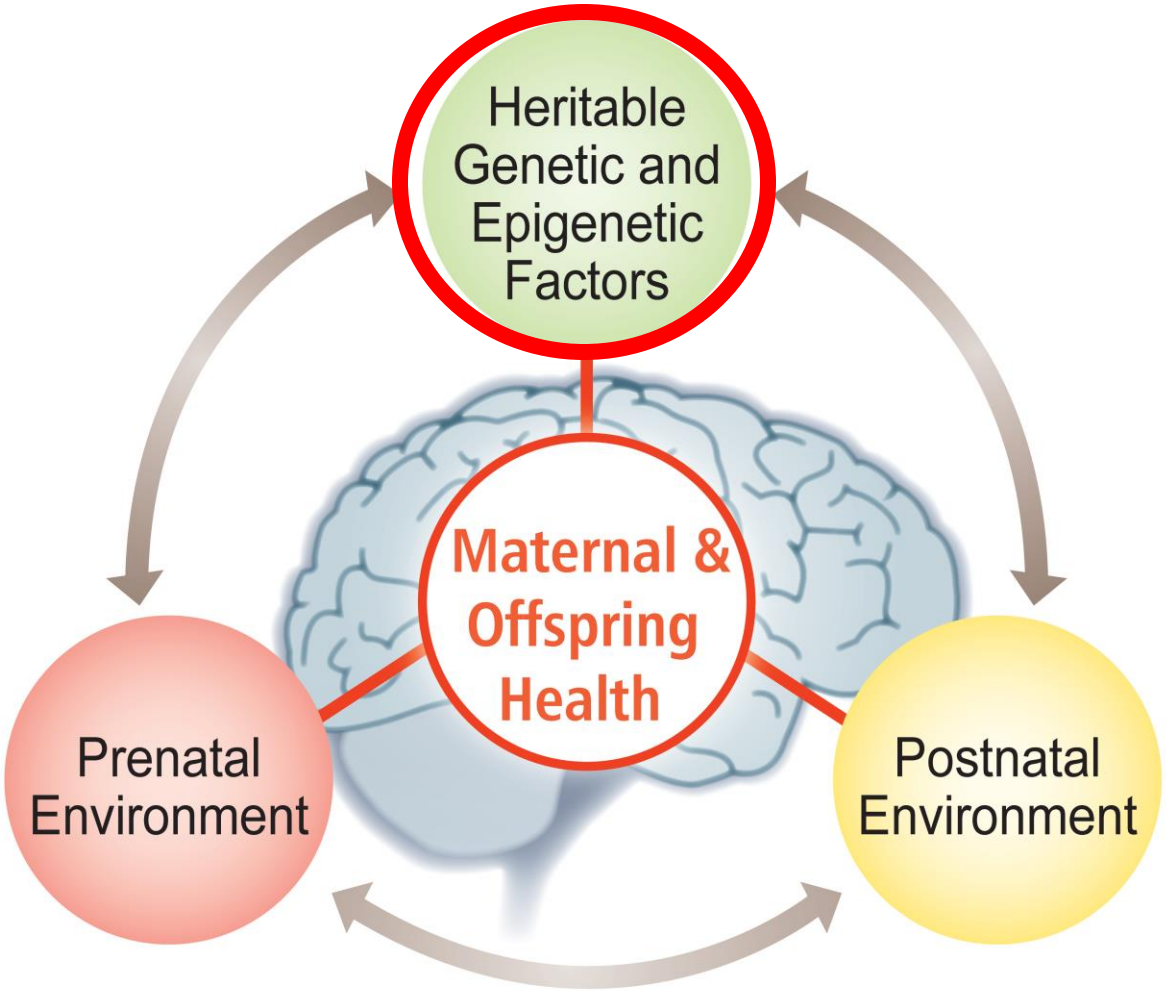

Does Stress Program Maternal and Offspring Health?

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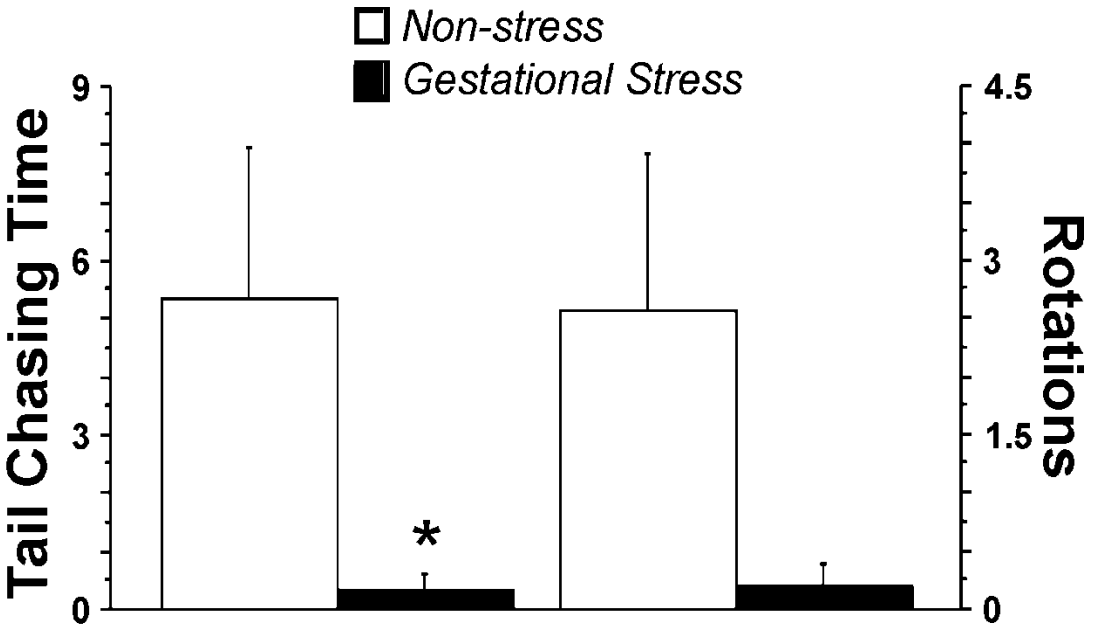
Gestational Stress Disrupts Maternal Behaviour



Zucchi et al., PLoS ONE, 2013

Can Stress During Pregnancy Influence Preterm Birth Risk?

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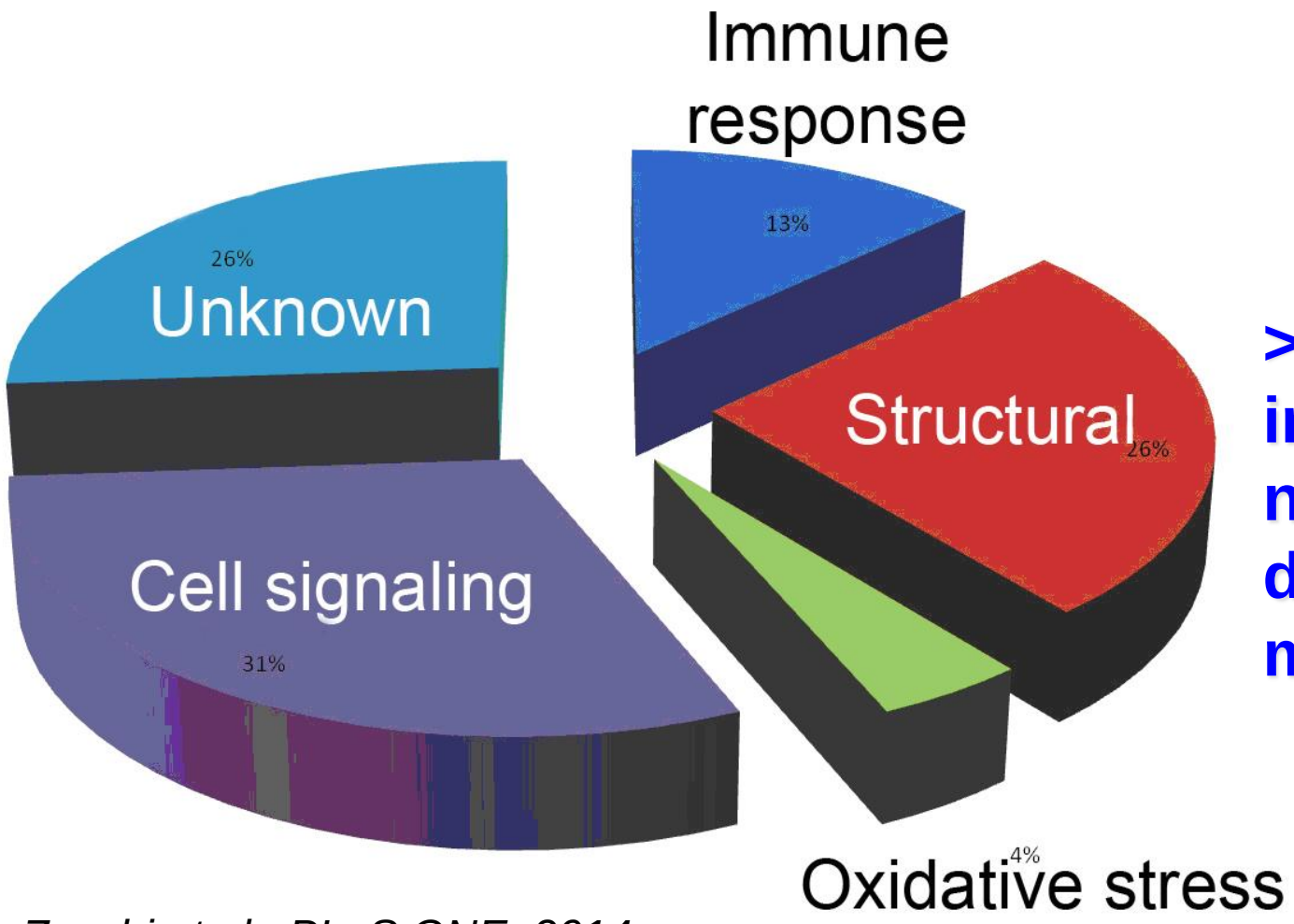
No Change in Gestational Length...

Prenatal Stress Programs Gene Expression Patterns



> 80 genes involved in neurological diseases and mental illness

Zucchi et al., PLoS ONE, 2014

Gestational Stress Alters Potentially Heritable Epigenetic Markers

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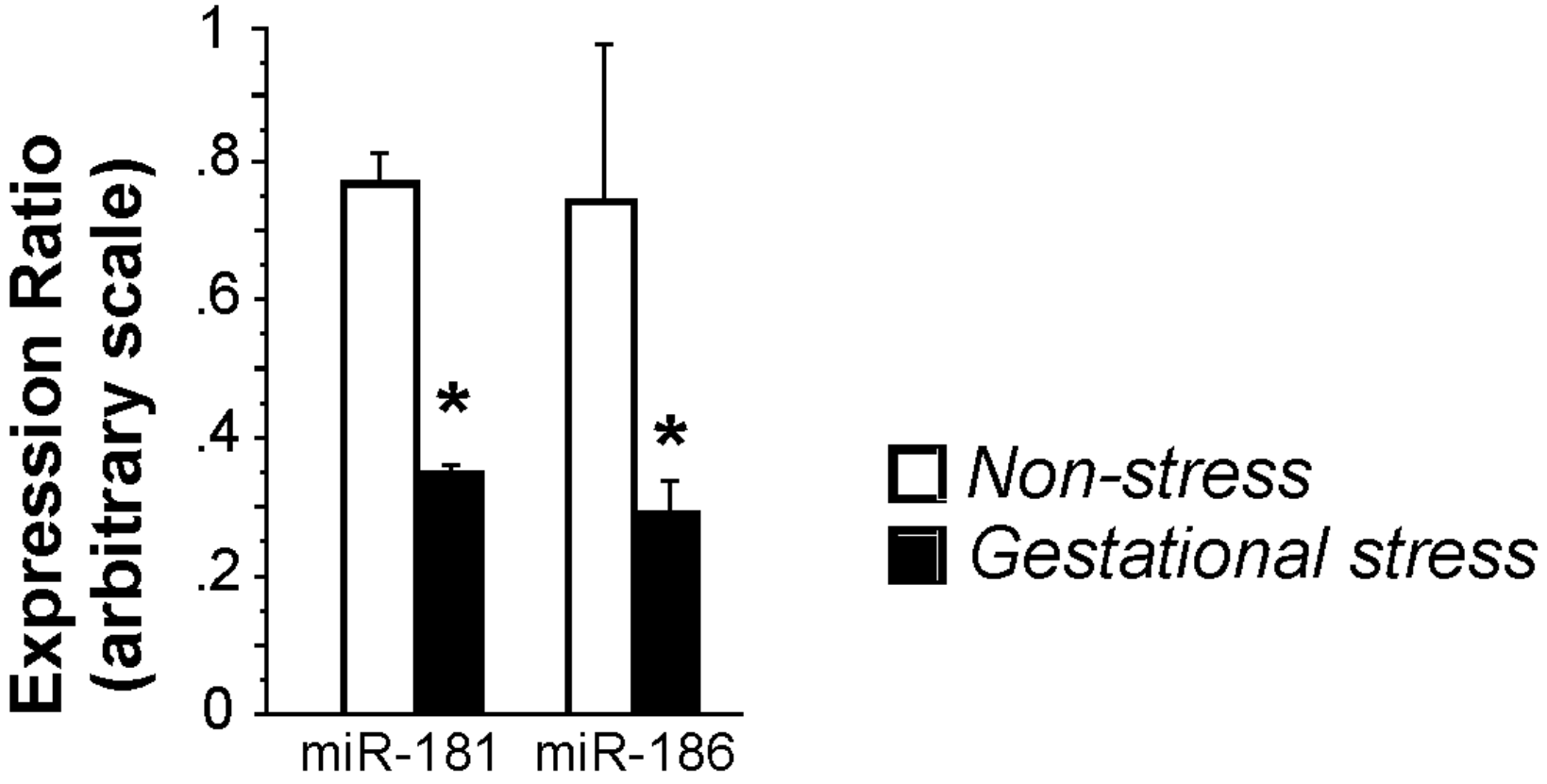

Zucchi et al., PLoS ONE, 2013

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Can Stress Effects Propagate to the Next Generations?

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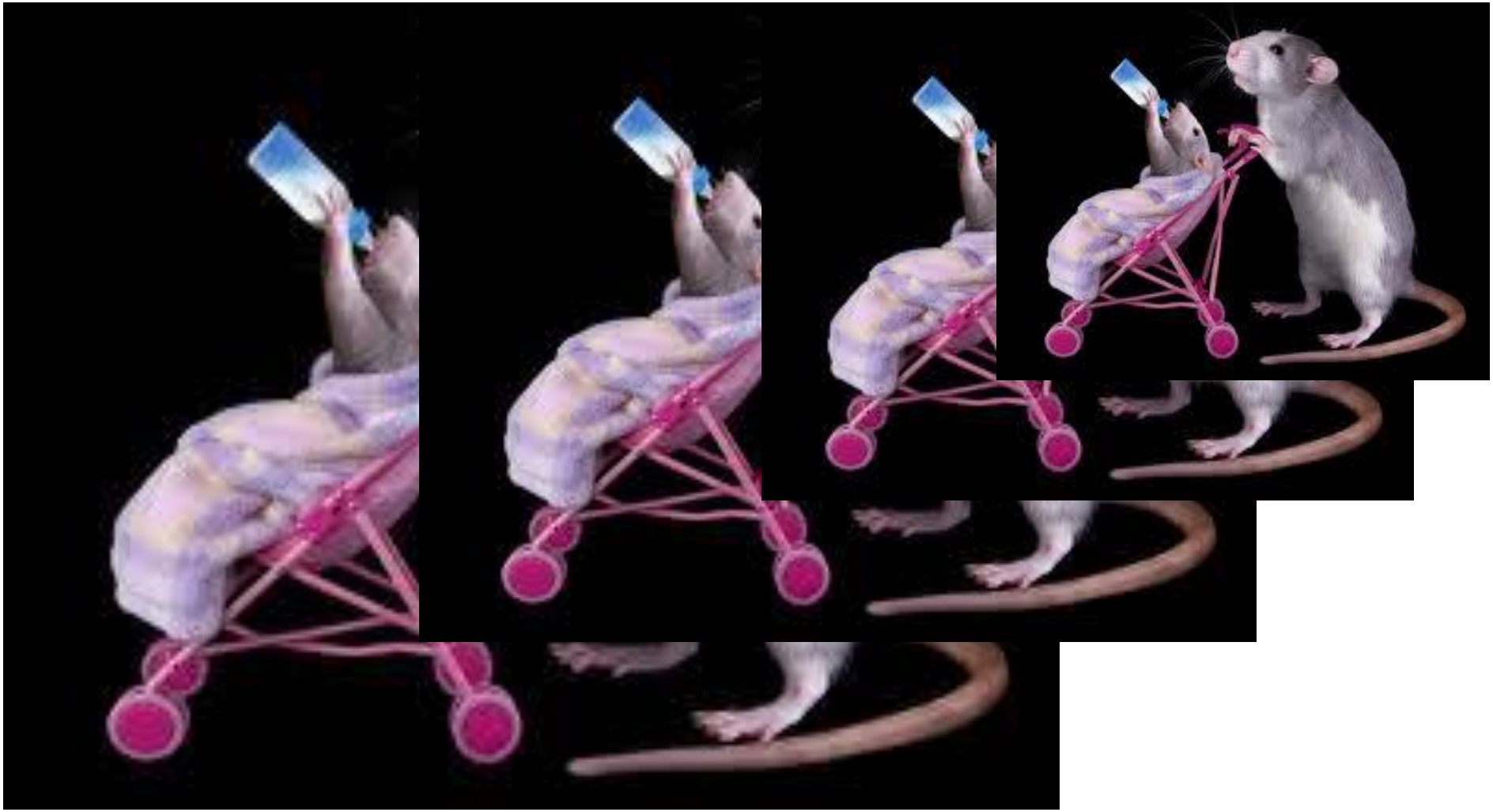
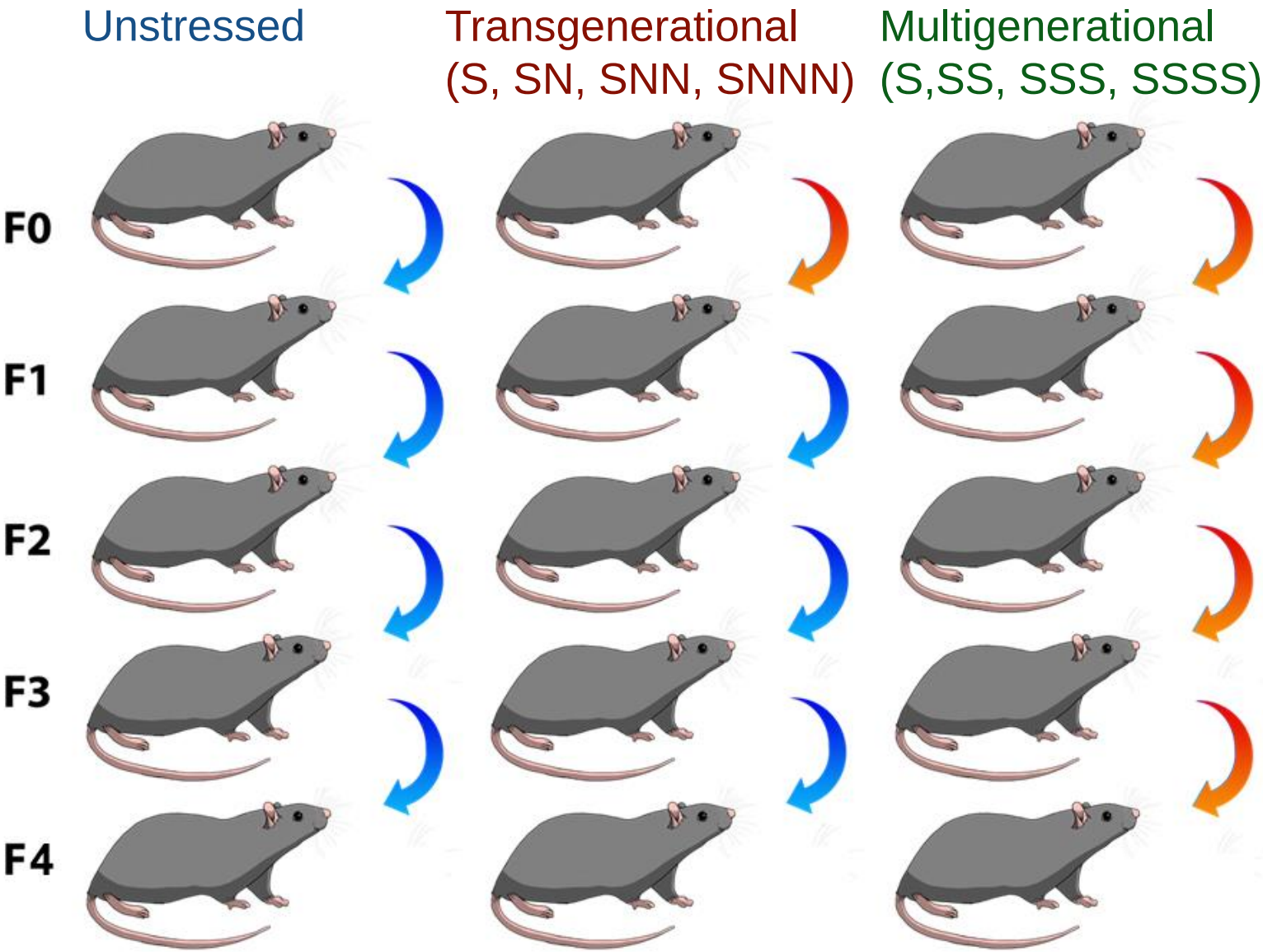


Model of Transgenerational Maternal Stress



Ancestral Stress Shortens Gestational Length

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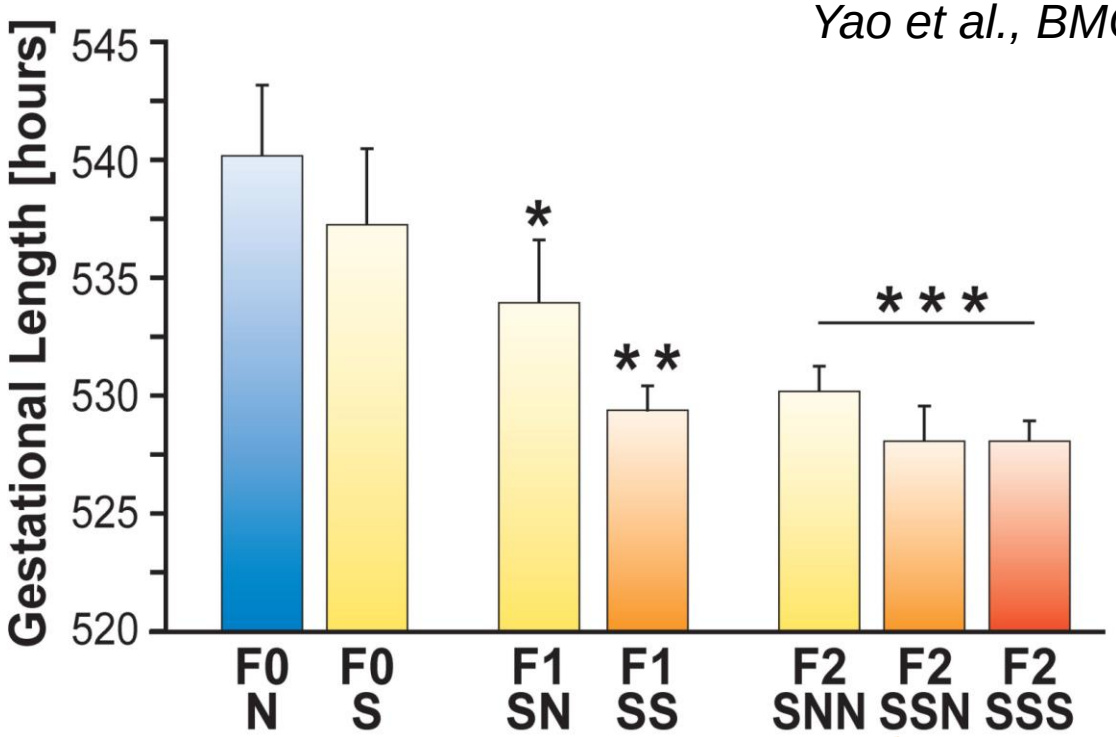
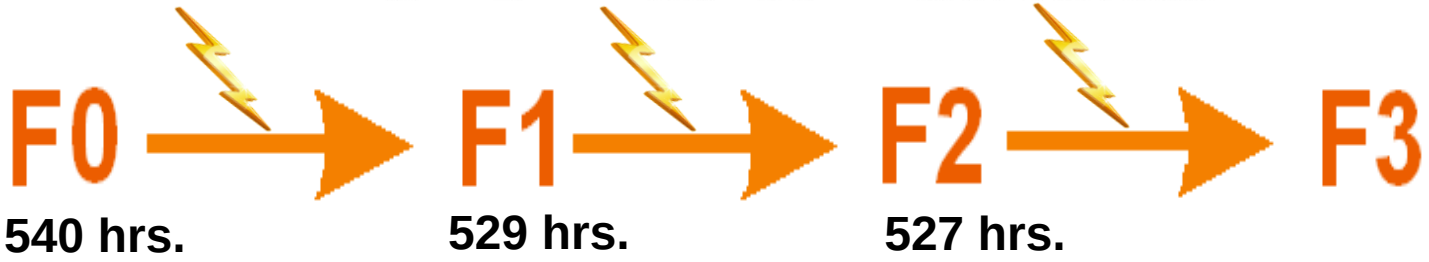
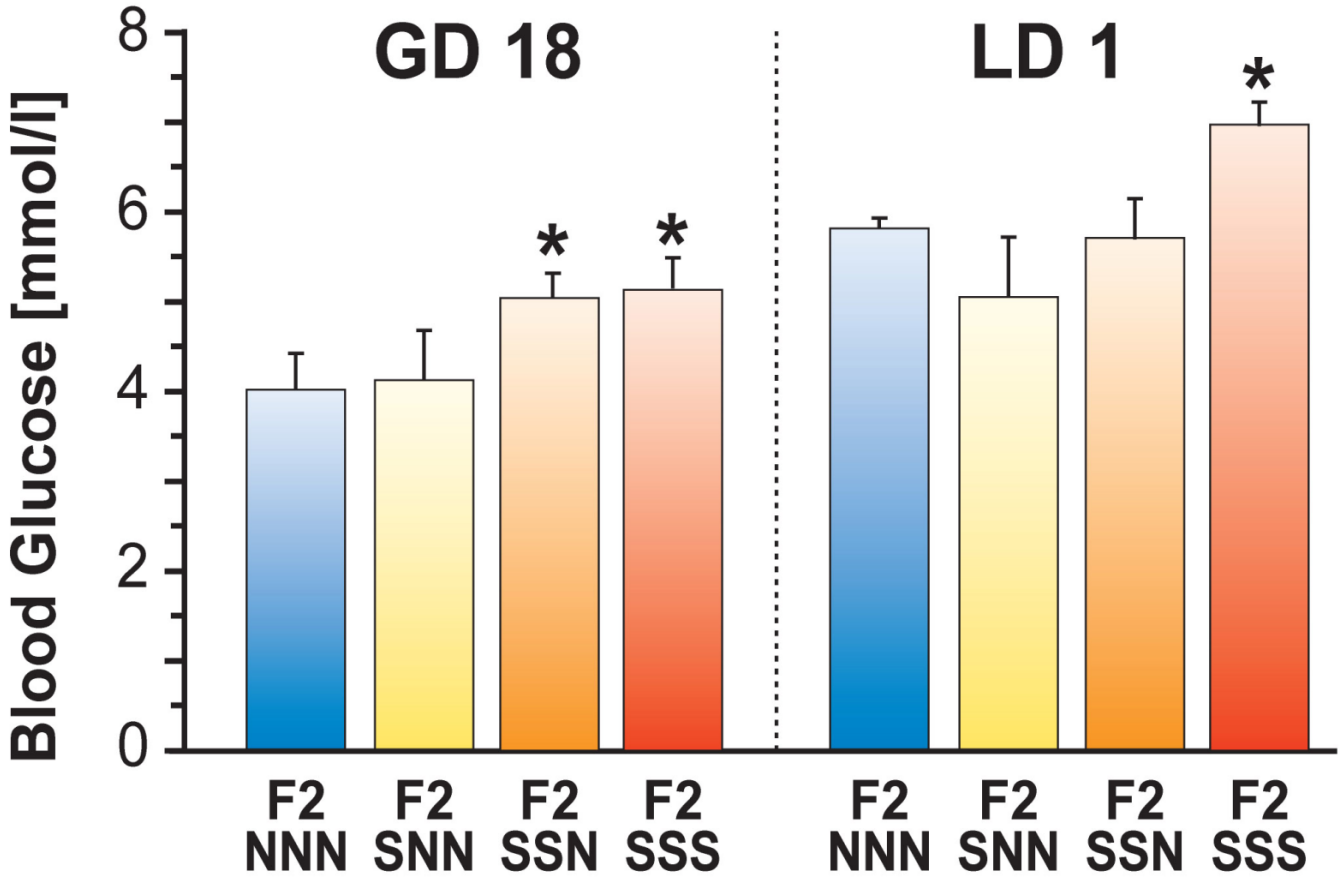
Yao et al., BMC Medicine, 2014





Ancestral Stress Elevates Blood Glucose Levels



Yao et al., BMC Medicine, 2014

Ancestral Stress Regulates the miR-200 Family: Role in Pregnancy Maintenance

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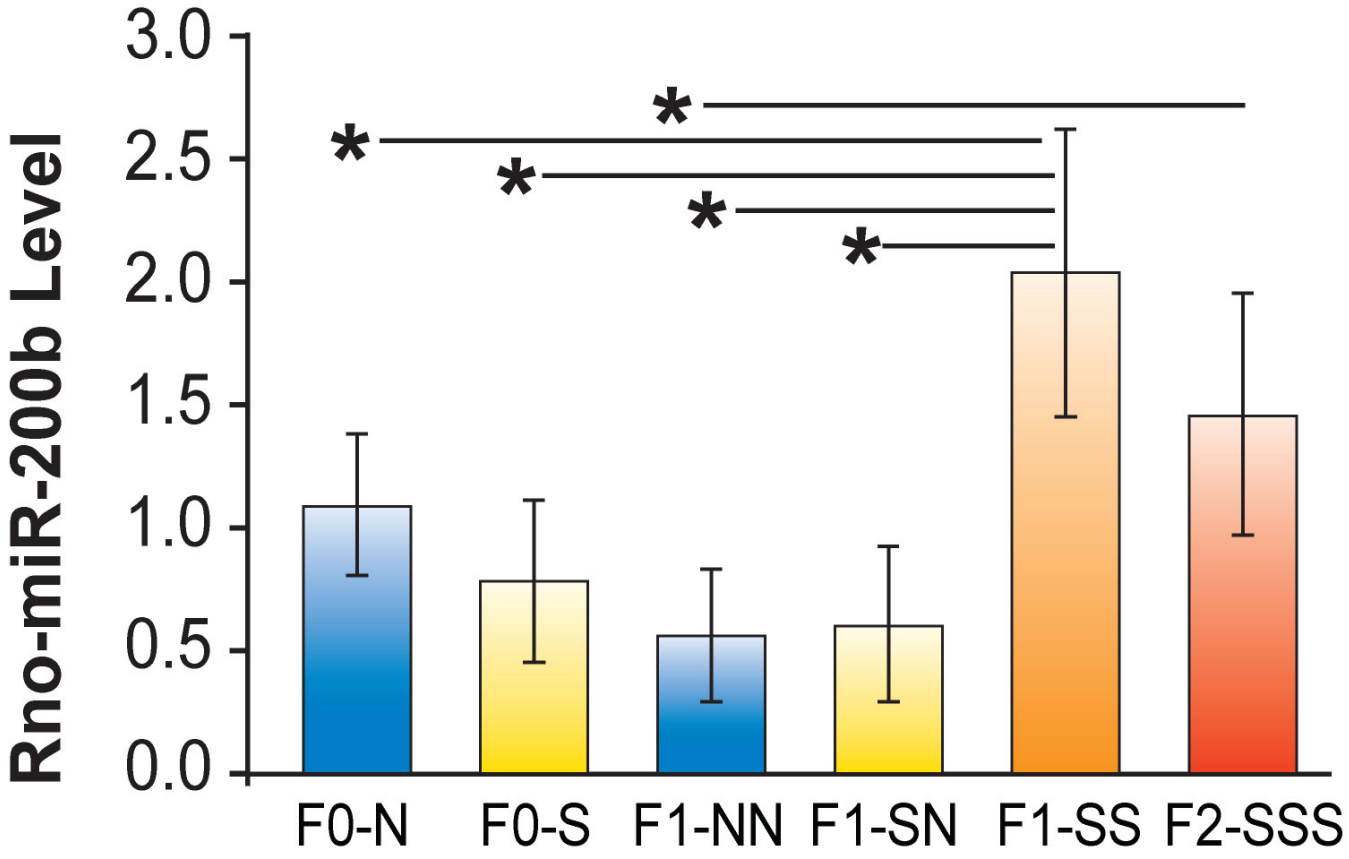
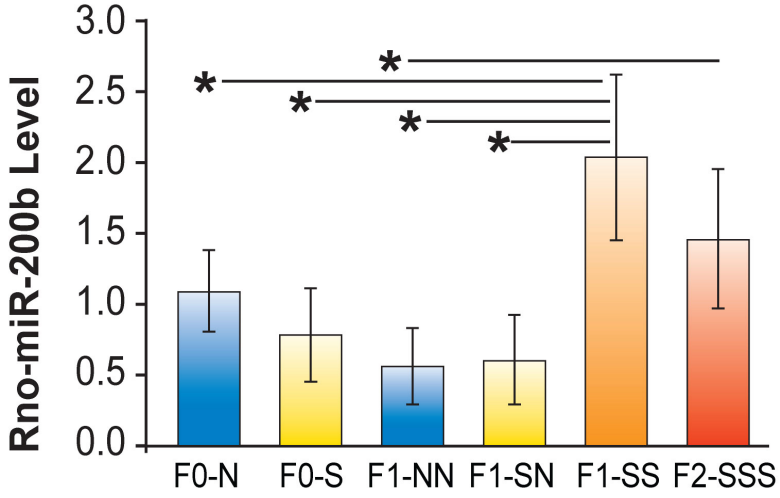
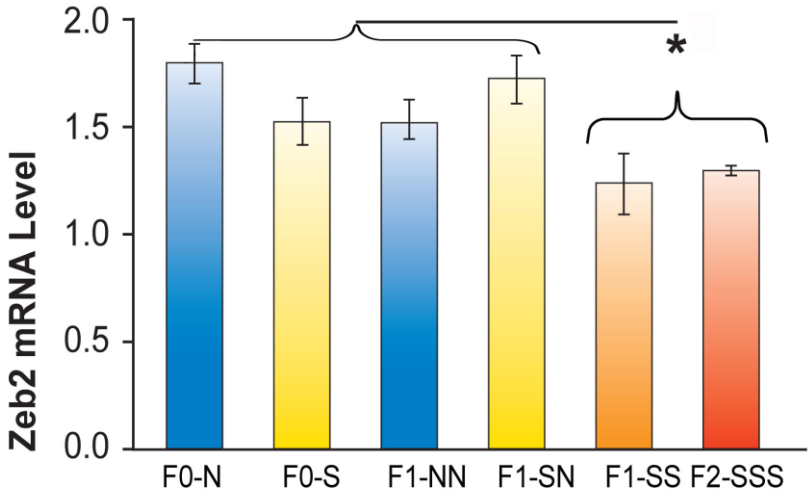
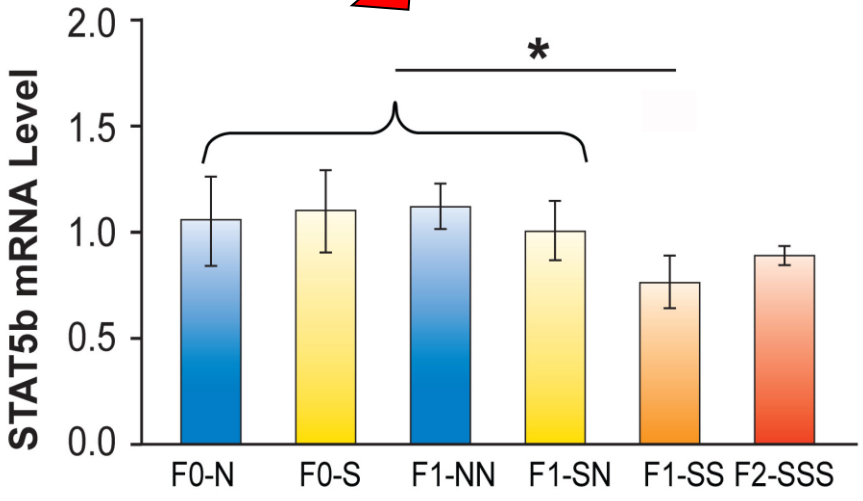


Yao et al., BMC Medicine, 2014

miR-200 Family Regulates Genes Involved in Pregnancy Maintenance







Yao et al.,
BMC Medicine, 2014

Placental microRNA Signatures as Proxies for Brain and Uterine Health

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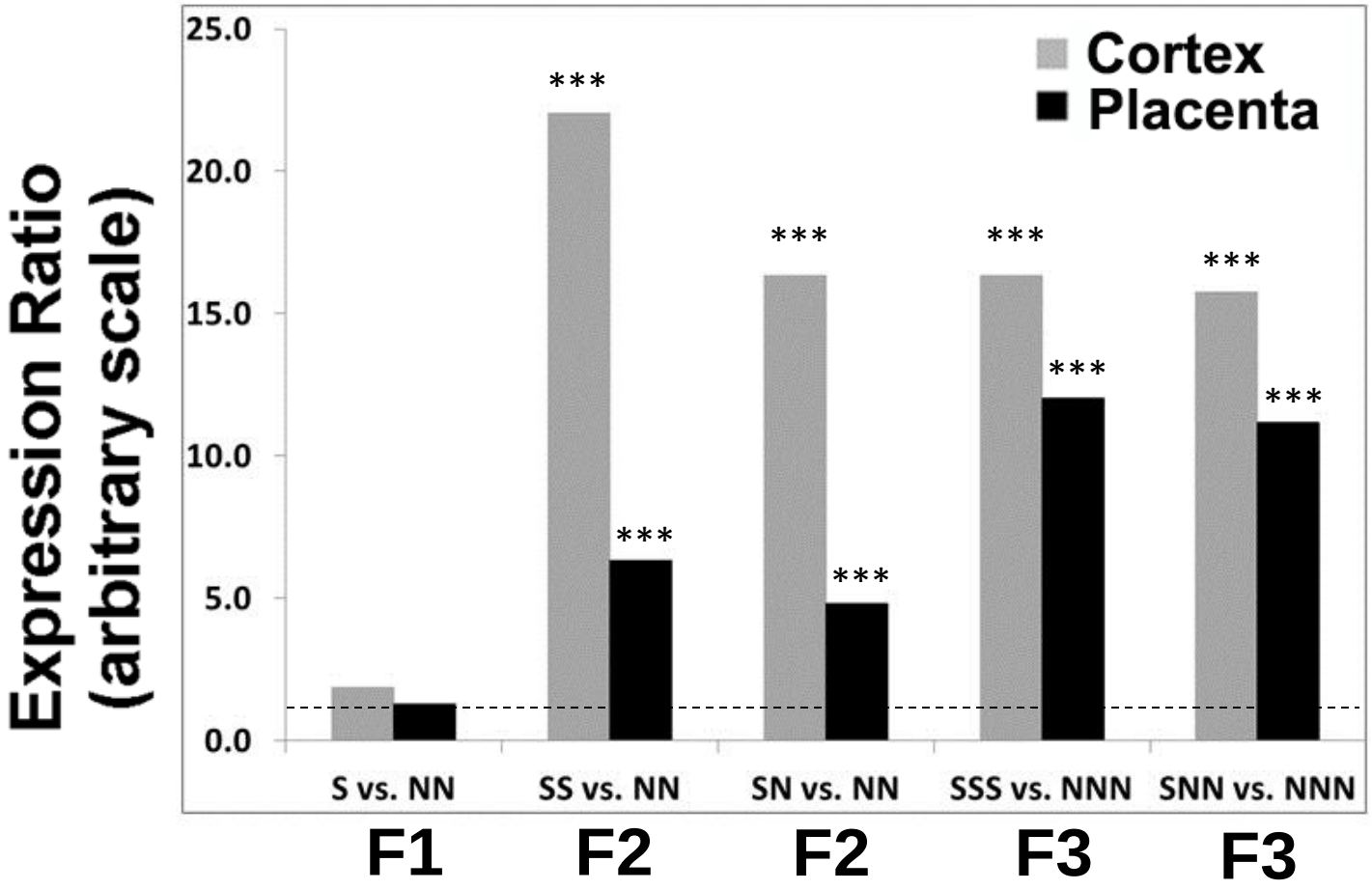
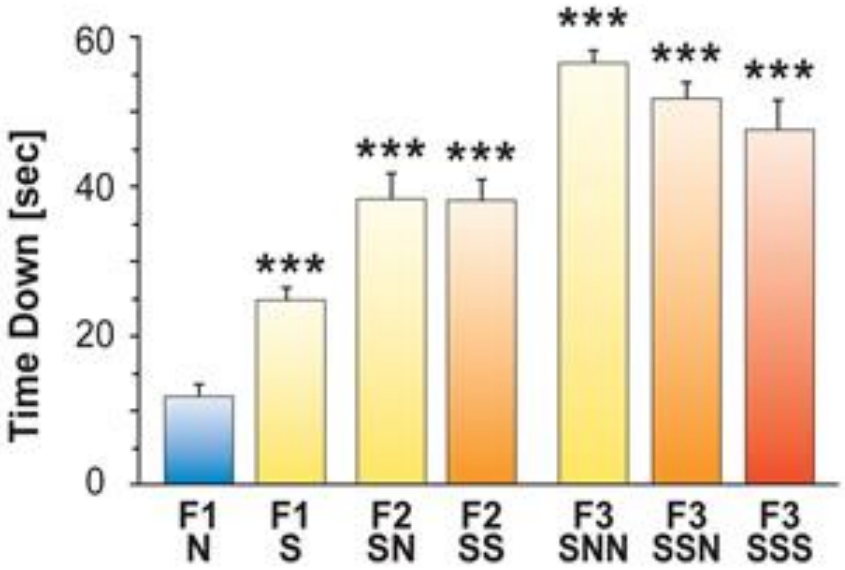


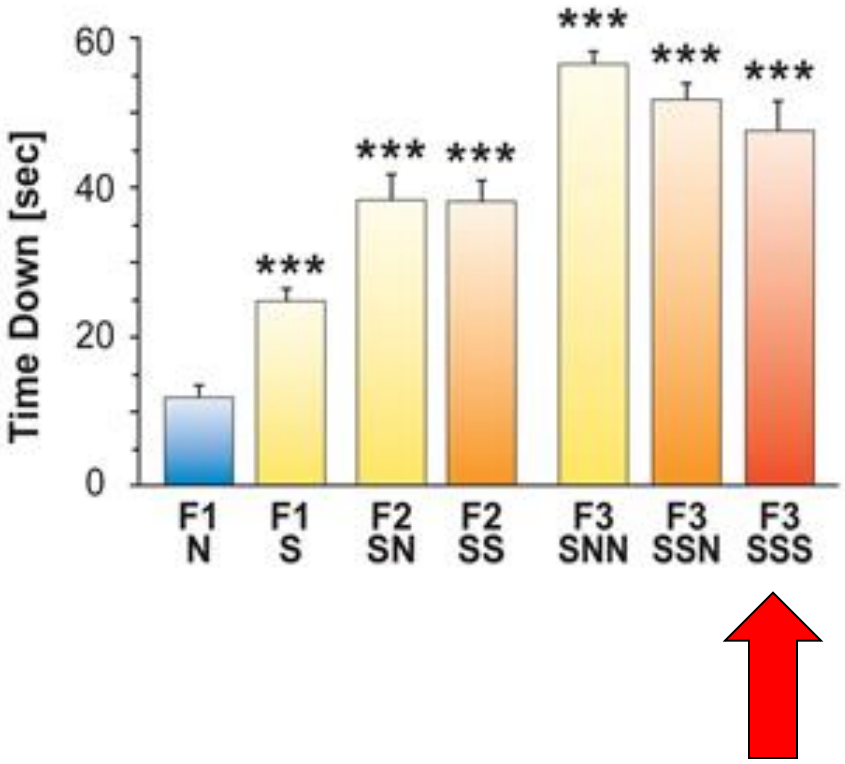
Babenko, Kovalchuk et al., unpublished data

Ancestral Stress Impedes Offspring Development



Yao et al., BMC Medicine, 2014

Ancestral Stress Impedes Offspring Development



Yao et al., BMC Medicine, 2014

Ancestral Stress Alters Behaviour During Vulnerable Periods in Life

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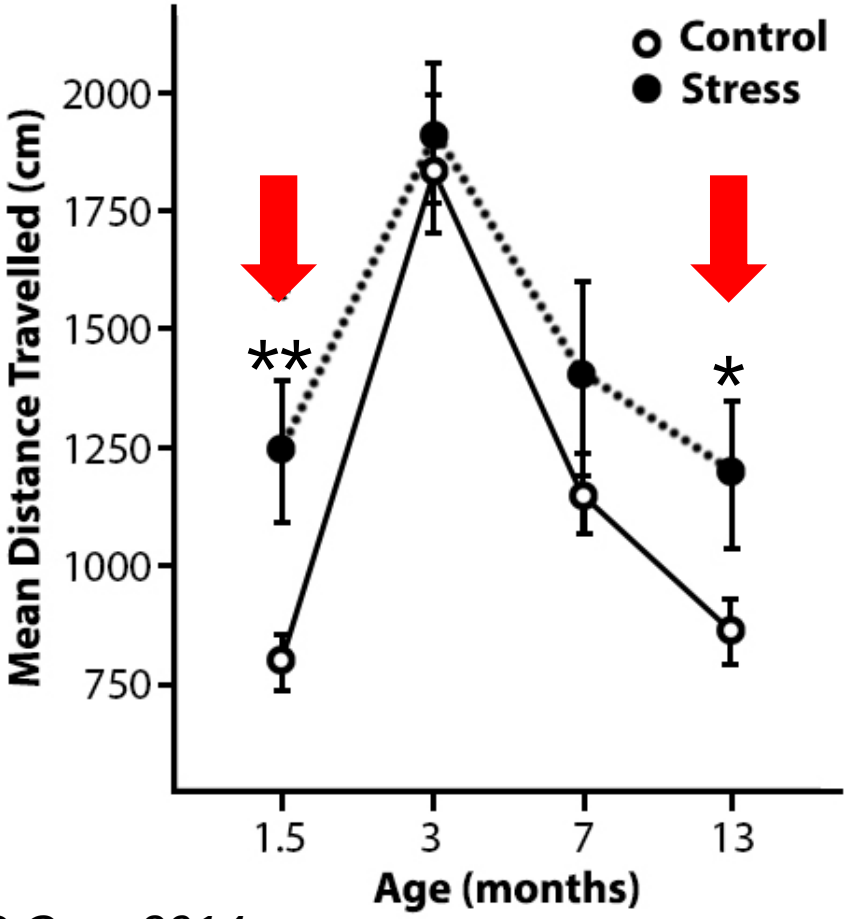

Erickson et al., PLOS One, 2014

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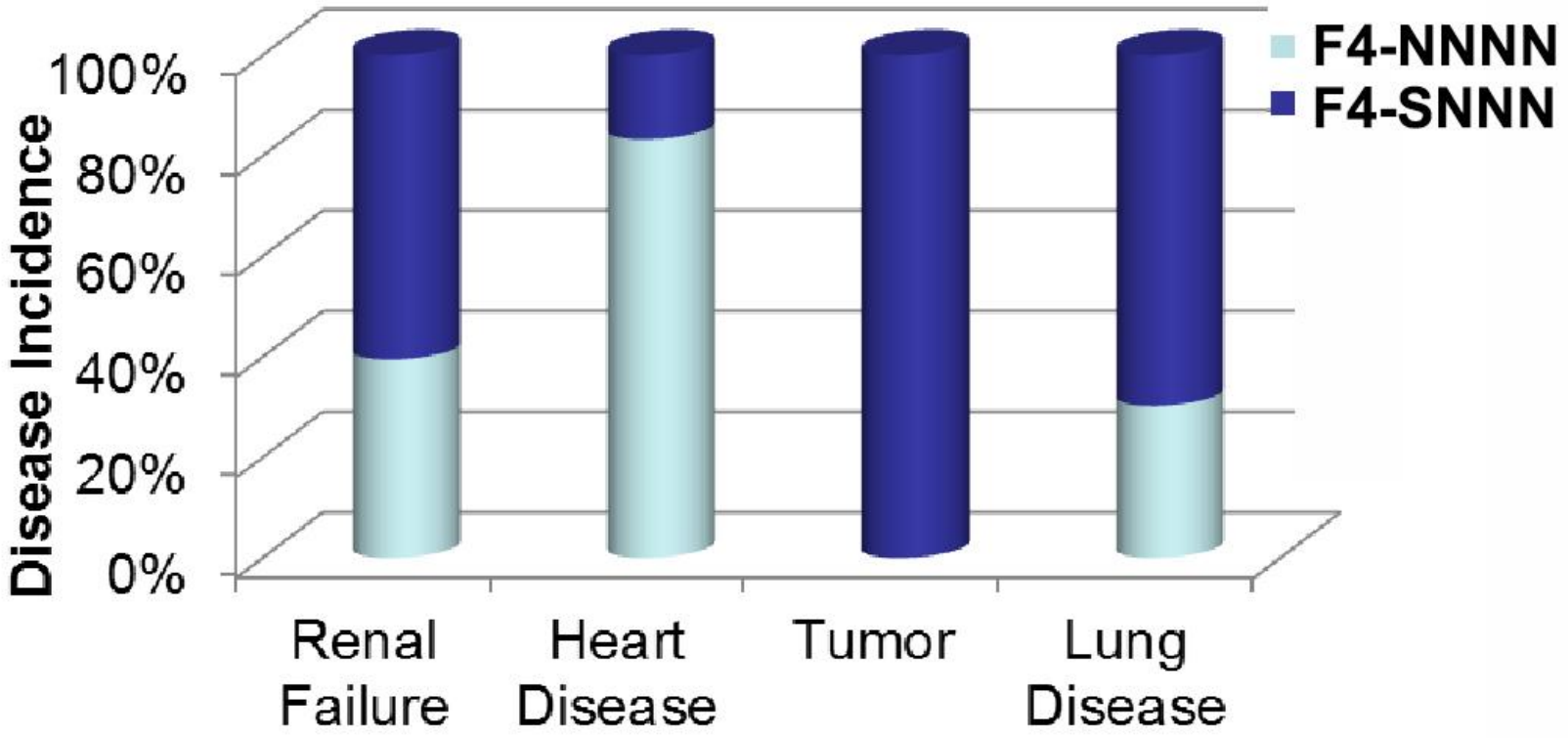
Remote Ancestral Stress Shifts Patterns of Complex Diseases



Ambeskovic et al., unpublished data

Can Beneficial Experience Offset Adverse Programming?

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Environmental Enrichment Mitigates Adverse Programming by Stress

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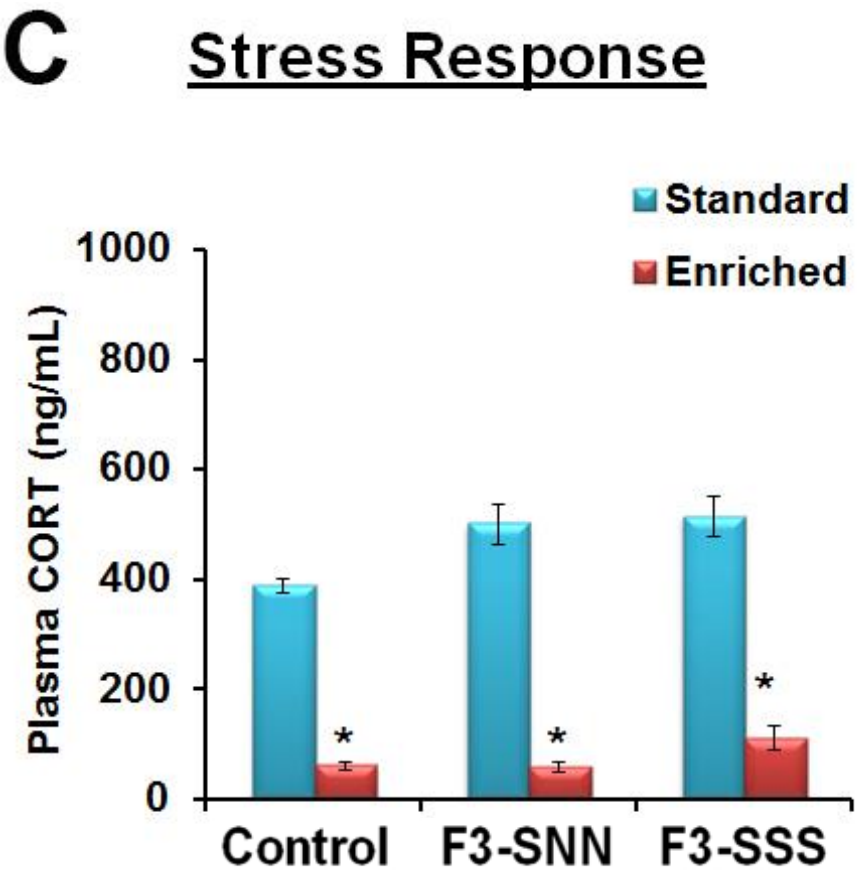

McCreary, Erickson, et al., unpublished data

Environmental Enrichment Mitigates Adverse Programming by Stress

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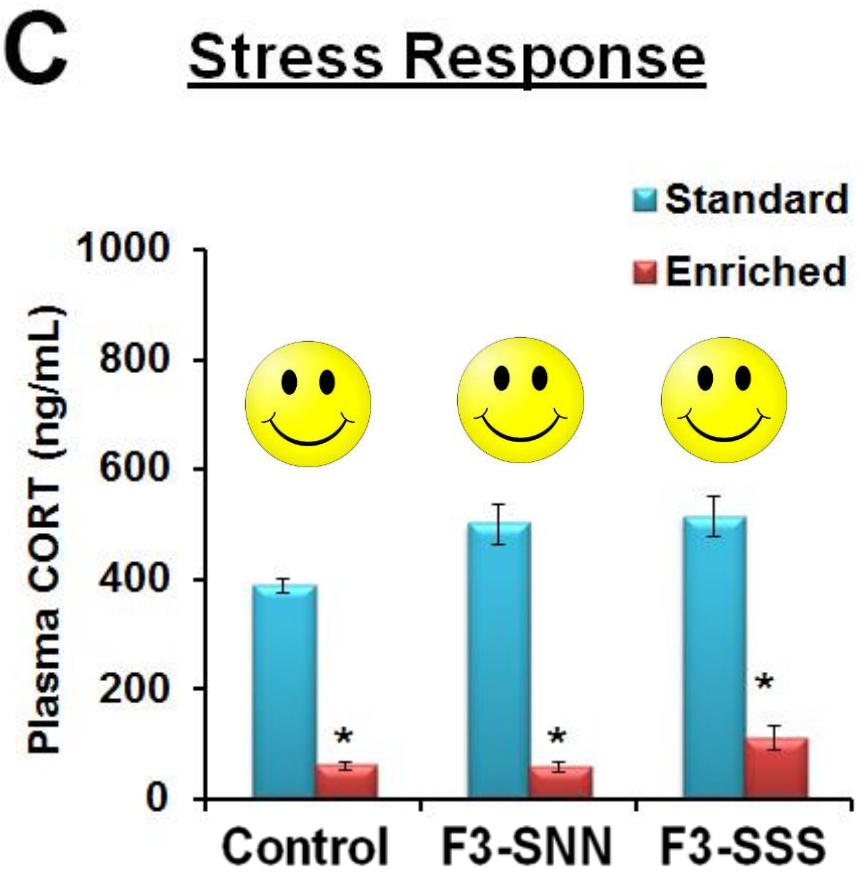

McCreary, Erickson, et al., unpublished data

Ancestral Stress May Better Prepare Future Generations

Benefits

- Resilience
- Metabolic Preparation

?????

Ancestral Stress Also Bears Health Risks

Benefits

- Resilience
- Metabolic Preparation

?????

Risks

- Cardiovascular
- Metabolic
- Aging

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Transgenerational Programming of Maternal and Offspring Health

Benefits

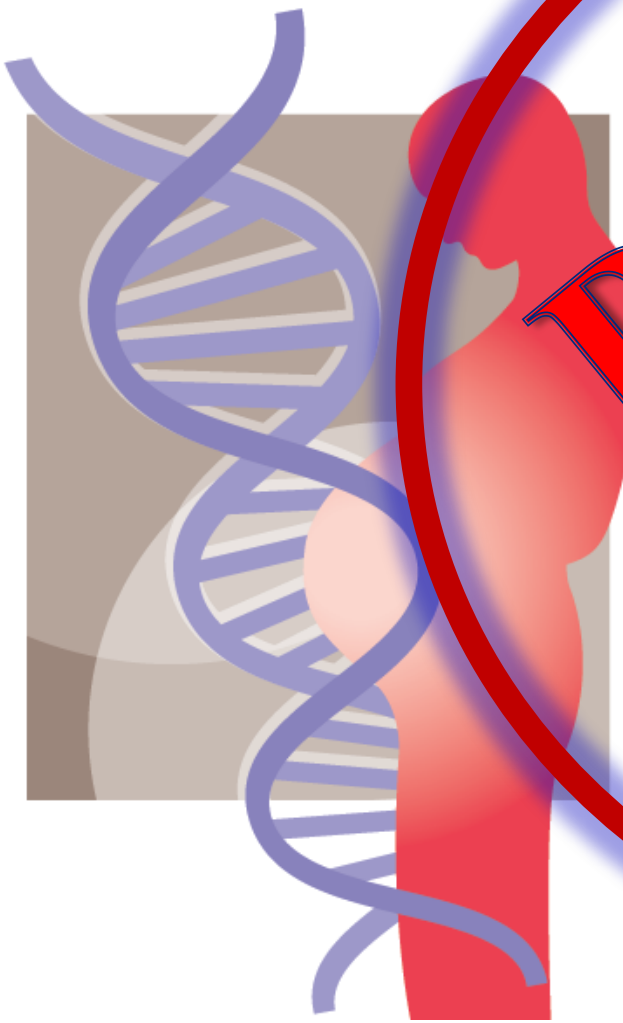
- Resilience
- Metabolic Preparation

Biomarkers

Risks

- Cardiovascular
- Metabolic
- Aging

Transgenerational Programming of Maternal and Offspring Health



Predict & Prevent

Benefits

- Resilience
- Metabolic
- Preparation

Biomarkers

Risks

- Cardiovascular
- Metabolic
- Aging

Building the Foundation for Healthy Futures

University of Lethbridge

- Ancestral stress is a significsnt influence on lifetime health trajectories.
- Transgenerational inheritance involves epigenetic mechanisms.
- Transgenerational studies may identify new predictive biomarkers of disease.

Acknowledgements

University of Lethbridge

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Tony Montina

Dept. of Biol. Sciences

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Dr. Olga Kovalchuk

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- Dr. Suzanne King (McGill University)

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Fondation canadienne pour l'innovation

Natural Sciences and Engineering Research Council of Canada
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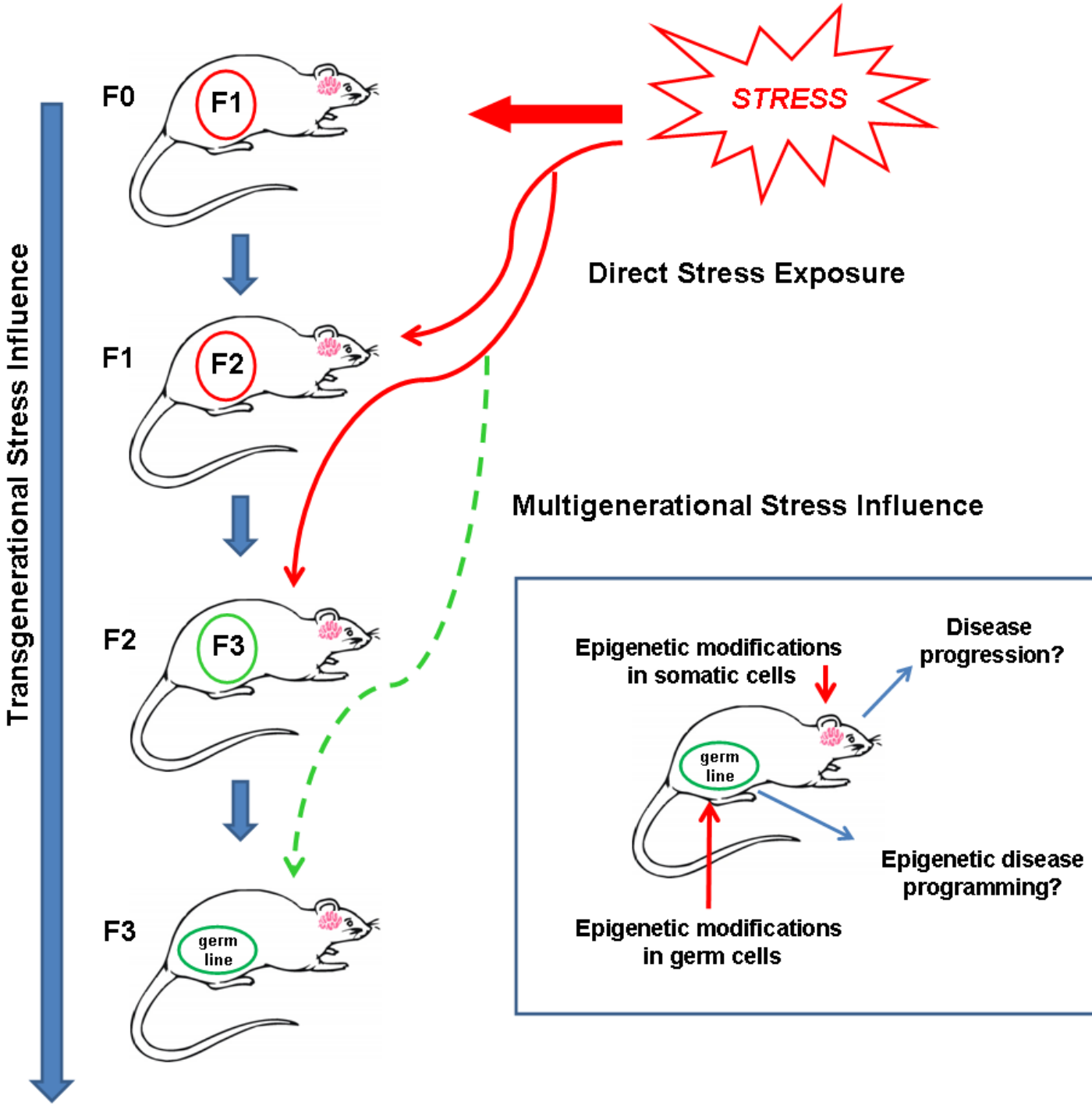
PreHOT
Preterm Birth and Healthy Outcomes Team

Alberta Innovates - Health Solutions

CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

Questions?

Does Stress Induce Genuine Trans-generational Effects?



Programming of the Stress Response

Great Great Grandmother

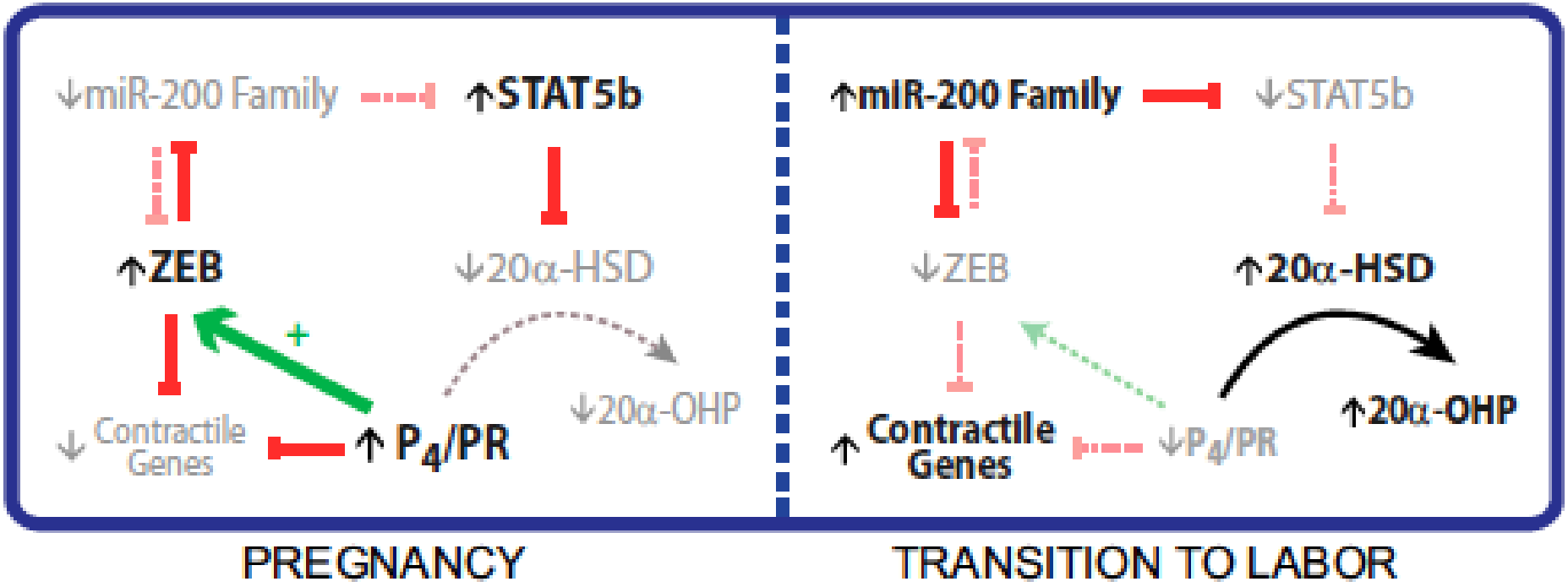
Great Grandmother

Grandmother

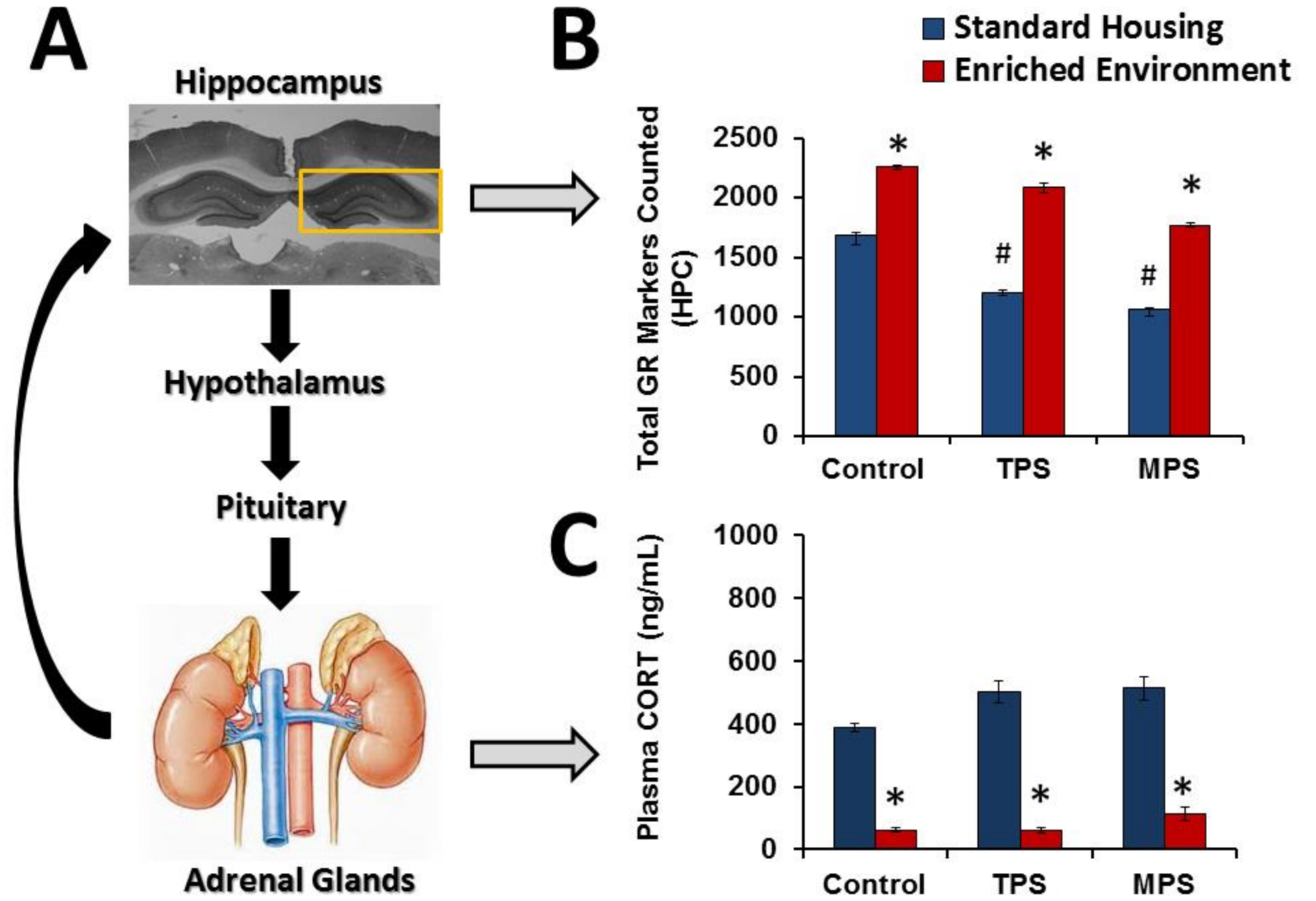
Mother

Proposed Mechanisms of Action of miR-200

Proposed mechanisms of action of miR200, ZEB1,2 and STAT5b - Carole Mendelson Lab



Williams et al., PNAS, 2012; 109:7529-34


A
Hippocampus
Hypothalamus
Pituitary
Adrenal Glands
B
Standard Housing
Enriched Environment
Total GR Markers Counted (HPC)
2500
2000
1500
1000
500
0
Control
TPS
MPS
C
Plasma CORT (ng/mL)
1000
800
600
400
200
0
Control
TPS
MPS

Transgenerational Epigenetic (microRNA) Programming of Cortical Development

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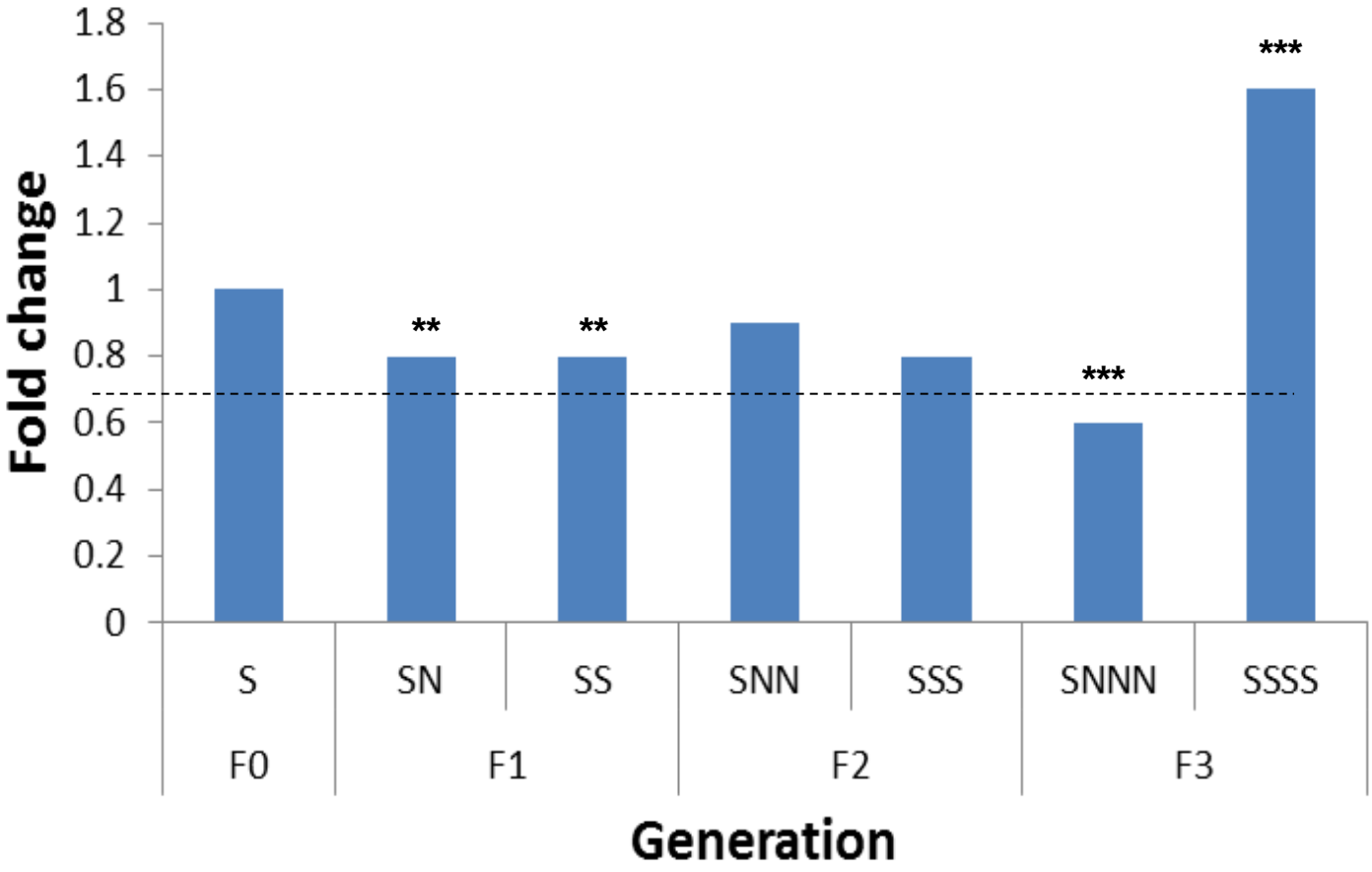
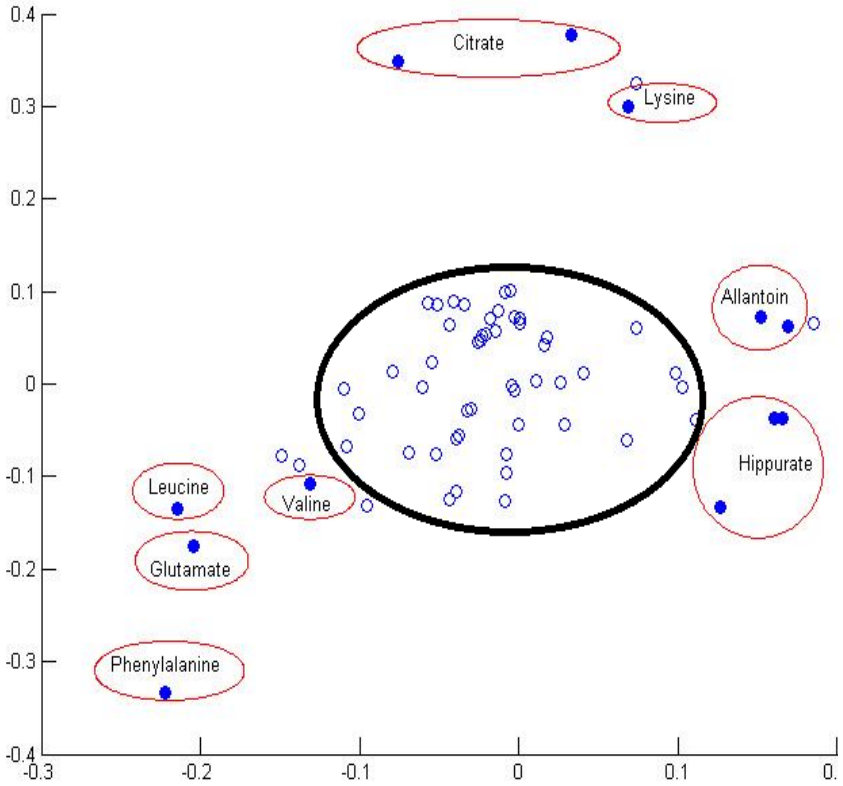
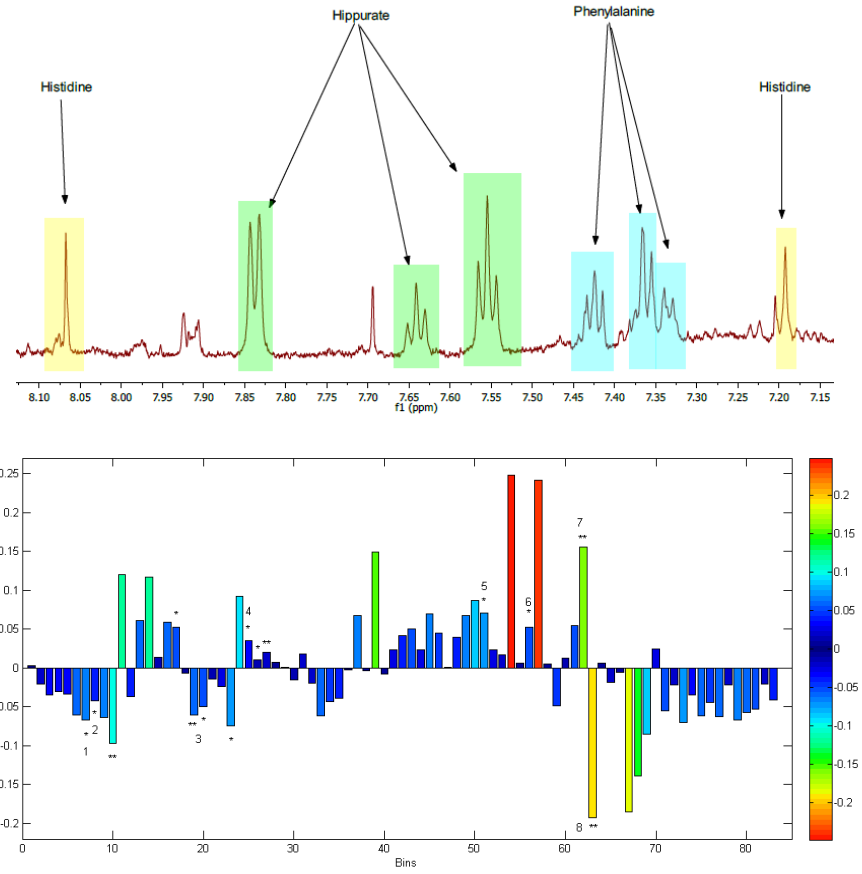


Babenko, Kovalchuk, et al., unpublished data

Down-Stream Metabolic Signatures of Stress





Example: F3-SNN

Kiss, Montina, et al., unpublished

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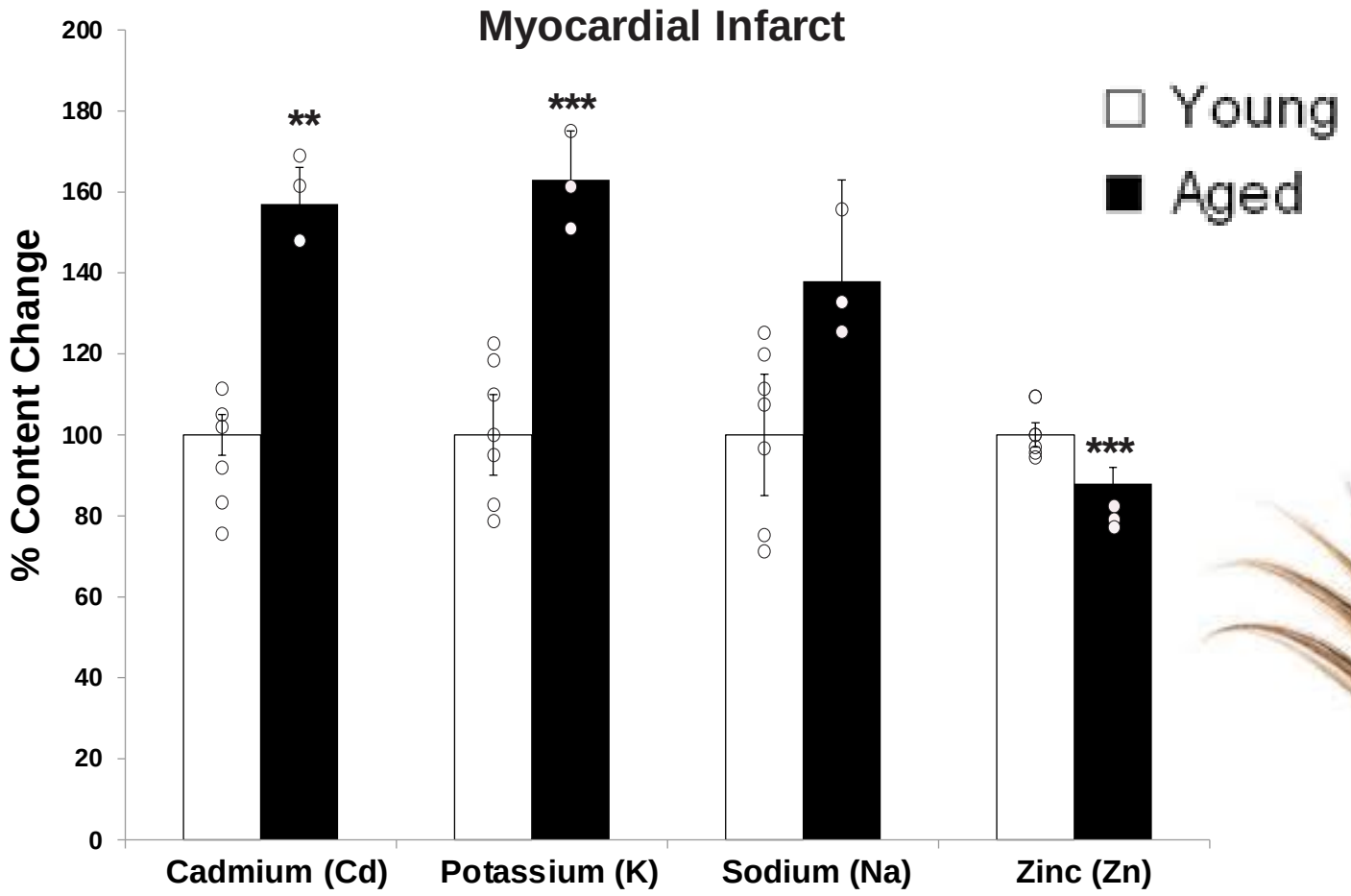
Metabolic Signatures of Age-related Diseases in Hair



Ambeskovic et al., 2013

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